ABSTRACT

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Real-time drug testing of paediatric diffuse midline glioma to support clinical decision making: The Zurich DIPG/DMG centre experience.

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BACKGROUND: Children diagnosed with diffuse midline gliomas (DMG) have an extremely poor overall survival: 9-12 months from diagnosis with currently no curative treatment options. Given DMG molecular heterogeneity, surgical biopsies are needed for molecular profiling and as part of enrolment into molecular-based and precision medicine type clinical interventions. In this study, we describe the results of real time profiling and drug testing at the diffuse intrinsic pontine glioma/DMG Research Centre at University Children's Hospital Zurich.
METHOD: Biopsies were taken using a frame based stereotactic robot system (NeuroMate®, Renishaw) at University Children's Hospital Zurich. Tissue samples were evaluated to confirm diagnosis by H3K27M and H3K27 trimethylation loss. Genomic analyses were done using a variety of platforms (INFORM, Oncomine, UCSF500 gene panel). Cell lines were developed by mechanical tissue dissociation and verified by either sequencing or immunofluorescence staining confirming H3K27M mutation and used afterwards for drug testing.
RESULTS: Twenty-five robot-assisted primary biopsies were successfully performed. Median hospital stay was 2 days (range 1-4 days). Nine low-passage patient-derived cells were developed, whereas 8 cell lines were used to inform response to clinically relevant drugs. Genome and RNA expression were used to further guide treatment strategies with targeted agents such as dual PI3K/mTOR inhibitor paxalisib.
CONCLUSION: We established a systematic workflow for safe, robot-assisted brainstem biopsies and in-house tissue processing, followed by real-time drug testing. This provides valuable insights into tumour prognostic and individual treatment strategies targeting relevant vulnerabilities in these tumours in a clinically meaningful time frame.

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